

## ORIGINAL PAPER

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## Psychopharmacoepidemiology in Iceland: effects of regulations and new medications

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**Abstract** The sale of psychotropic medications in Iceland has waxed and waned during the past 20 years with approximately 5 years between peak and bottom quantities sold. Apparently, it has decreased following restrictions imposed by the public health authorities and increased again following the introduction of new drugs. In order to study this further, all prescriptions for psychotropic medications to non-hospitalized inhabitants of the capital city (Reykjavík) and dispensed by pharmacists there during 1 month in 1984, 1989 and 1993 were analysed in order to estimate the 1-month prevalence of psychopharmacological use. The results support the hypothesis partly as prescriptions for tranquillizers decreased in 1989 as well as the amount of tranquillizers and hypnotics prescribed following new restrictions, whereas the prevalence odds ratio of obtaining prescriptions for hypnotics remained unchanged. The proportion of patients receiving excessive amounts of tranquillizers and/or hypnotics decreased. The prevalence of excessive use of these drugs (i.e. >90 DDD/month) was 0.5% in 1993. In 1993 the prevalence of the use of antidepressants as well as the amount prescribed had increased substantially following the introduction of the new selective serotonin reuptake inhibitor medications. Thus, the prevalence of patients obtaining any psychotropic medication remained unchanged from 1984 to 1993.

**Key words** Psychopharmacological drug use · Prescriptions · Prevalence · Tranquillizers · Hypnotics · Antidepressants

### Introduction

The use of psychotropic medications increased in many countries until the mid- or late 1970s, with a subsequent reduction in the amount used, especially that of benzodiazepines (Allgulander 1986; Greenblatt et al. 1983). Following an initial general welcome, negative attitudes towards their use developed during the 1970s and 1980s, after reports of withdrawal symptoms following therapeutic dosages of benzodiazepines (Covi et al. 1973; Fruensgaard 1976; Pétursson and Lader 1981). In contrast, the use of antidepressant medications has been increasing (NLN 1990; NLN 1993) and to some extent possibly replacing the use of benzodiazepines (Zoëga et al. 1992).

The first of the new antidepressants, the selective serotonin reuptake inhibitors (SSRI), were registered in Iceland in 1988. The cost of these new antidepressants has become a major concern of the public health authorities, as it has inflated the total cost of antidepressants by 340% from 1989 to 1995. In 1989 the SSRI drugs accounted for 15% of the total cost of antidepressants and in 1995 for no less than 73% of the total cost (Heilbrigðis- og tryggingamálaráðuneytið 1995).

Excessive and unnecessary use of any form of medication is of course to be condemned. But it is highly regrettable that too many individuals with mental disorders do not seek treatment, and that too many of those doing so do not procure treatment that is effective or adequate (Beardsley et al. 1988; Eisenberg 1992). Various attempts have been made to influence both the prescription habits of doctors and the demand by patients for psychotropic medications. These attempts include educating family doctors about positive diagnoses of psychiatric disorders and the importance of effective and sufficient treatment (Rutz et al. 1990), establishing by legislation approved indications for use of certain medications (Shorr et al. 1994) as well as supplying doctors and patients with information about side effects and possible dependence on or abuse of psychotropic medications. Registration of therapeutic drugs and regulations by public health authorities limiting the

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amount which can be given on any one prescription have been an effective means for controlling the use of medications (Ólafsson et al. 1980; Weintraub et al. 1991; Zoëga et al. 1992). Further regulations limiting reimbursement of the cost of medication from the national health service or insurance companies may have a controlling effect on prescriptions and drug use (Soumerai et al. 1987). Limiting reimbursement of doctors fees may have an opposite effect.

The prevalence of prescriptions for benzodiazepines and antidepressants has been found to increase with age (Nolan and O'Malley 1988; Joukamaa et al. 1995; Binge-fors 1996) and thus differ from that of mental disorders identified by the General Health Questionnaire (Helgason 1991) and from that found in the ECA studies (Regier et al. 1988). Primary care physicians prescribe by far the majority of psychotropic medications (Beardsley et al. 1988), often in insufficient dosages and to older patients, than psychiatrists (Helgason 1992).

The main source of information about the use of psychotherapeutic drugs in Iceland is the published records on the sale of all drugs (Petersen 1987, 1989). The quantity sold is available in comparable units, daily defined dosis (DDD; NLN 1986), grouped according to the anatomical-therapeutic-chemical classification (ATC; 1991) since 1975. The sale of psychotherapeutic medications in Iceland has waxed and waned during the past 20 years. It was reduced by public health control measures from 113 DDD per 1000 total population per day in 1976 to 72 DDD/1000 per day in 1980. The sales increased again reaching 110 DDD/1000 per day in 1985 as the sale of hypnotics almost doubled following the introduction of new hypnotics in 1980. It decreased again to 85 DDD/1000 per day in 1989 when the DDD of triazolam had been reduced by one half in 1986 to 0.25 mg (Petersen 1987), and it had been prohibited to prescribe more than 30 DDD at the same time of the most commonly used hypnotics (Heilbrigðis- og tryggingamálaráðuneytið 1988).

The use of antidepressants has increased gradually since 1980, but mainly from 1989 when the first SSRI antidepressants had been registered. Since that time the sale of antidepressants has increased from 14.9 DDD/1000 per day to 19.3 in 1993 and to 33.0 in 1995 when the total sales of psychopharmacological drugs was 105 DDD/1000 per day (Sigfússon and Magnússon 1993 (1996)). On the other hand, the sale of tranquillizers has continued to decrease. The use of neuroleptics has remained fairly constant over the past 20 years.

In order to contain the expenditure of the National Health Service on drugs, limitations have been set for their reimbursement during the past 10 years or so. From 1991 the cost of several drugs which the public health authorities thought were excessively used, including tranquillizers and hypnotics, has not been reimbursed by the National Health Insurance.

Previous studies of prescriptions to outpatients in Reykjavík have shown that the prescribed amount of drugs per 1000 inhabitants there was very similar to the sales figures for the whole country, except for neurolep-

tics (Zoëga et al. 1992). The prescribed amount for the latter was less than one half of the sales figures since neuroleptics were mainly used for inpatients.

The purpose of the present paper is to study changes in the use of psychotropic medications and to evaluate the effects of regulations intended to limit their use and of the introduction of new drugs. This was done by analysing prescriptions for psychopharmacological drugs to outpatients in order to compare the 1-month prevalence rates of psychopharmacological drug use and the quantities dispensed.

## Materials and methods

In collaboration with the health insurance and the pharmacies in Reykjavík all prescriptions for psychotropic medications to outpatients living in Reykjavík were collected during the month of March in the years 1984, 1989 and 1993. The number of patients was 4818, 4982 and 5240, respectively. However, one pharmacy responsible for 5–6% of all prescriptions in 1984 and 1989 could not, for technical reasons, supply information in 1993. The prescriptions had information on the gender and age of the patients, the amount prescribed as well as the name of the prescribing physician whose speciality could then be ascertained. Some of this information was missing on a few prescriptions which were therefore not included in the statistical analysis. The prescriptions were grouped according to the ATC classification (NLN 1986; ATC 1991). The amount of each drug prescribed was transformed into standard units, daily defined doses (DDD), as they were in 1984 (NLN 1986), e.g. chlorpromazine 300 mg, diazepam 10 mg and amitriptyline 75 mg. The DDD for drugs registered after 1984 are also included (ATC 1991), e.g. fluoxetine 20 mg. Thus, it is possible to compare the prescribed amount of medications in each ATC group in comparable units. Stimulants such as amphetamine and methylphenidate are not included in the analysis, as they were prescribed only to a handful of individuals with special permits. Children under the age of 15 years are not included in the prevalence estimates, as they were rarely treated with psychopharmacological methods.

Prevalence rates and their standard errors were calculated in the usual manner (Daly et al. 1991).

Apart from morbidity, confounding factors, such as gender, age and speciality of physicians, influence the possible changes in the number of patients prescribed different psychotherapeutic medications over time. Each patient may receive different types of drugs and may obtain prescriptions from more than one type of specialist. In order to get around this the prescriptions were categorized by speciality of physicians and type of drug by ATC group according to the following hierarchies. Each patient is entered only once into the model in the following order. According to speciality: a) psychiatrist; b) primary care physician; c) internist; and d) other physicians. According to type of drug: a) neuroleptics; b) antidepressants; c) tranquillizers; and d) hypnotics. These hierarchies divide the patients into disjointed groups where each individual belongs to exactly one group. Data for each patient can thus be presented with a multivariate binary vector  $Y$ . The prevalence odds ratios of obtaining these medications were then estimated by use of log-linear models for counts (McCullagh and Nelder 1989). By using these models, confounding factors such as those mentioned previously are controlled for and the development of prevalence odds ratios over time is analysed and corrected for these variables and their two-way interactions. Higher-order interactions were also examined, but as their effect was minimal, prevalence odds ratios can be presented by the formula:

$$\exp(\theta_j + \theta_{jk} Y_k),$$

where  $\theta_j = \log$  odds for  $Y = 1$  and  $\theta_{jk} = \log$  odds describing the association between the  $Y_j$  and the  $Y_k$  coordinates (Diggle et al. 1994).

Permissions for the studies were granted by the commission for the protection of personal data.

## Results

Each patient received on average 1.6–1.8 prescriptions per month, 1.1 for antidepressants and 1.4 for tranquillizers. Approximately 25% of the patients got more than one type of medication. The most common combination was tranquillizers and hypnotics (14%), similar in all 3 years, whereas only 2% of patients got both neuroleptics and antidepressants.

The restriction of the amount of hypnotics which can be given on any one prescription, as well as the effect of decreasing the DDD of triazolam, resulted in a reduction in the proportion of patients receiving more than 30 DDD during 1 month in 1989 to one half of what it was in 1984. At the same time the proportion of patients obtaining more than one prescription during 1 month increased by approximately one third. The proportion of patients who got more than 90 DDD of tranquillizers and/or hypnotics during 1 month decreased significantly from 11.3% in 1984 to 9.3% in 1989 and 8.0% in 1993 ( $\chi^2 = 3.88$ ,  $df = 2$ ,  $p < 0.0001$ ). The 1-month prevalence of excessive use of these drugs thus defined was 0.5% in the adult population in 1993. Two thirds of the patients obtaining antidepressants received more than 1 month's supply measured in

DDD. This is explained partly by the fact that the DDD of tricyclic antidepressants is considerably less than the average effective therapeutic dosage for depressive disorders.

Psychiatrists prescribed psychopharmacological drugs to 12% of the patients each year, whereas 58–65% of patients had obtained their prescriptions from primary care physicians. Psychiatrists prescribed multiple psychopharmacological drugs to their patients to a greater extent than other physicians, on average 1.6 and 1.4 drugs per prescription in 1984 and 1993, respectively, compared with 1.2 drugs prescribed by other physicians in both years.

The overall prevalence (Table 1) of patients obtaining any psychotropic medication has remained fairly similar from 1984 to 1993, whereas the DDD/1000 per day decreased slightly (Table 2). There was a significant decrease in the prevalence of use of tranquillizers from 1984 to 1989, as well as in the DDD/1000 population aged 15 years or more. The prevalence of psychopharmacological drug use increased with age in a similar way in all 3 years (Fig. 1), as indeed did the DDD/1000 per day, peaking around the age of 80 years. However, the prevalence increased for the elderly in 1989 and 1993 over that in 1984, whereas there was a slight decrease in the DDD/1000 per day in all age groups except the very elderly.

The prevalence for neuroleptics decreased slightly, although hardly to a significant degree, whereas the DDD/1000 per day remained fairly constant. On the other hand, the prevalence for hypnotics increased especially between

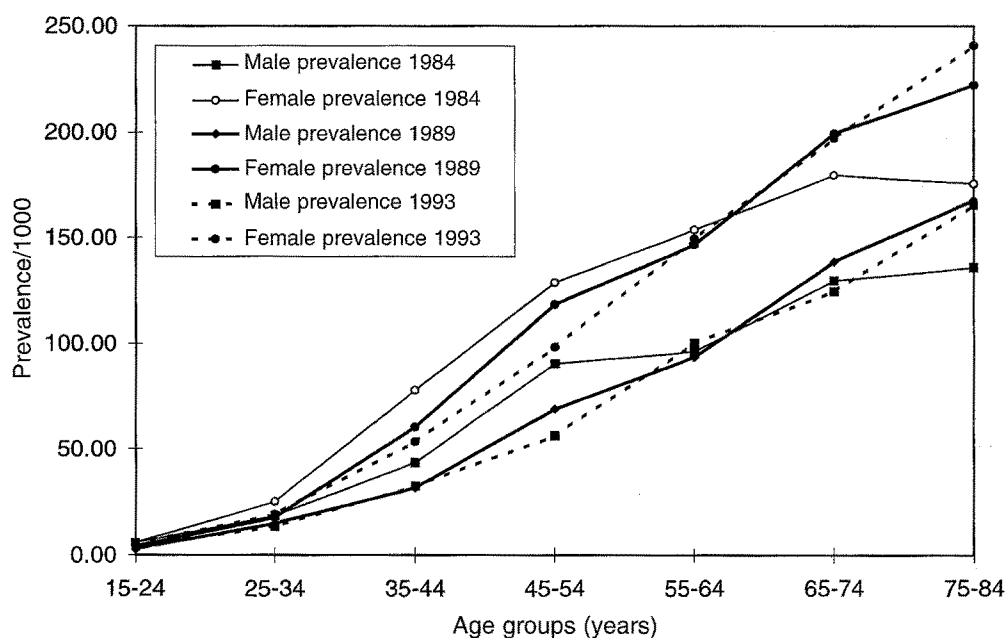
**Table 1** One-month prevalence of patients obtaining psychotropic medications per 1000 population aged 15 years and older in 1984, 1989 and 1993 by gender and Anatomical – Therapeutic – Chemical classification (ATC) groups

ATC group	Prevalence per 1000 population											
	Males						Females					
	1984		1989		1993		1984		1989		1993	
	‰	SE	‰	SE	‰	SE	‰	SE	‰	SE	‰	SE
Neuroleptics	6.1	0.43	4.2	0.35	4.9	0.36	7.5	0.46	6.9	0.42	6.4	0.39
Antidepressants	7.0	0.46	7.9	0.47	9.8	0.50	11.8	0.57	15.5	0.63	19.7	0.69
Tranquillizers	31.3	0.96	25.7	0.84	24.7	0.80	50.7	1.16	42.5	1.03	41.0	0.98
Hypnotics	22.7	0.83	27.3	0.87	27.0	0.83	39.9	1.04	48.1	1.09	46.0	1.04
Any psychotropic medication	53.4	1.25	49.9	1.16	51.1	1.13	86.3	1.49	84.7	1.42	87.1	1.39

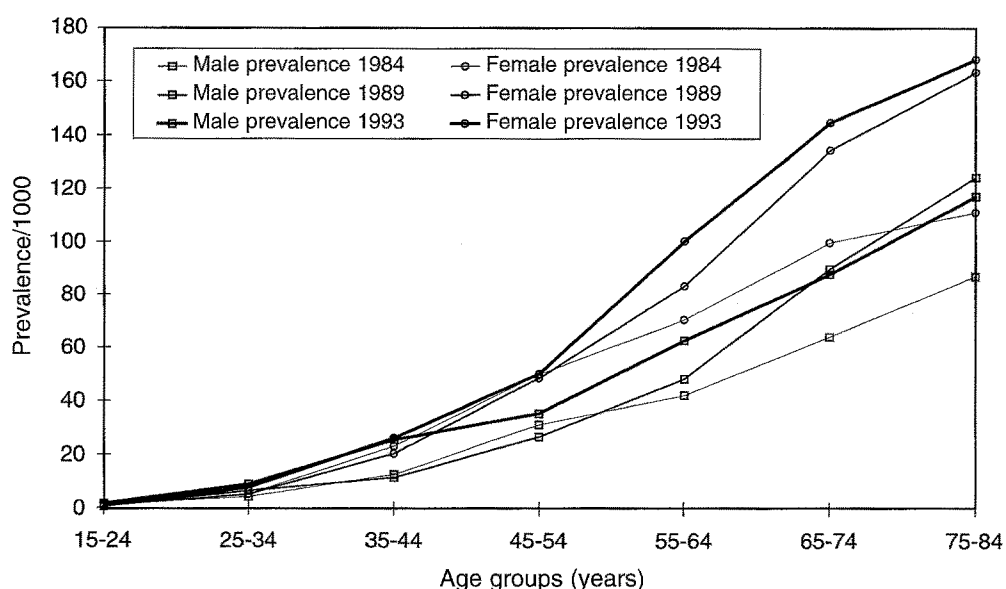
**Table 2** Daily defined doses for psychotropic medications per 1000 population aged 15 years and older per day (DDD/1000 per day) prescribed during 1 month in 1984, 1989 and 1993 by gender and ATC groups

ATC group	DDD/1000 per day											
	Males						Females					
	1984		1989		1993		1984		1989		1993	
	‰	SE	‰	SE	‰	SE	‰	SE	‰	SE	‰	SE
Neuroleptics	5.0	0.39	5.2	0.38	5.7	0.39	5.2	0.38	6.6	0.41	5.3	0.36
Antidepressants	10.5	0.56	13.9	0.62	18.4	0.69	17.3	0.69	27.6	0.84	35.2	0.91
Tranquillizers	33.9	1.00	28.9	0.89	27.0	0.83	50.2	1.16	44.7	1.06	41.7	0.99
Hypnotics	43.1	1.13	35.0	0.98	35.8	0.95	73.8	1.38	55.5	1.17	56.2	1.14
All psychotropic medications	92.5	1.60	83.0	1.47	86.9	1.45	146.5	1.87	134.4	1.74	138.4	1.70

**Fig. 1** One-month prevalence of patients obtaining psychotropic medications in Reykjavík in 1984, 1989 and 1993 by gender and age



**Fig. 2** One-month prevalence of patients obtaining hypnotics in Reykjavík in 1984, 1989 and 1993 by gender and age



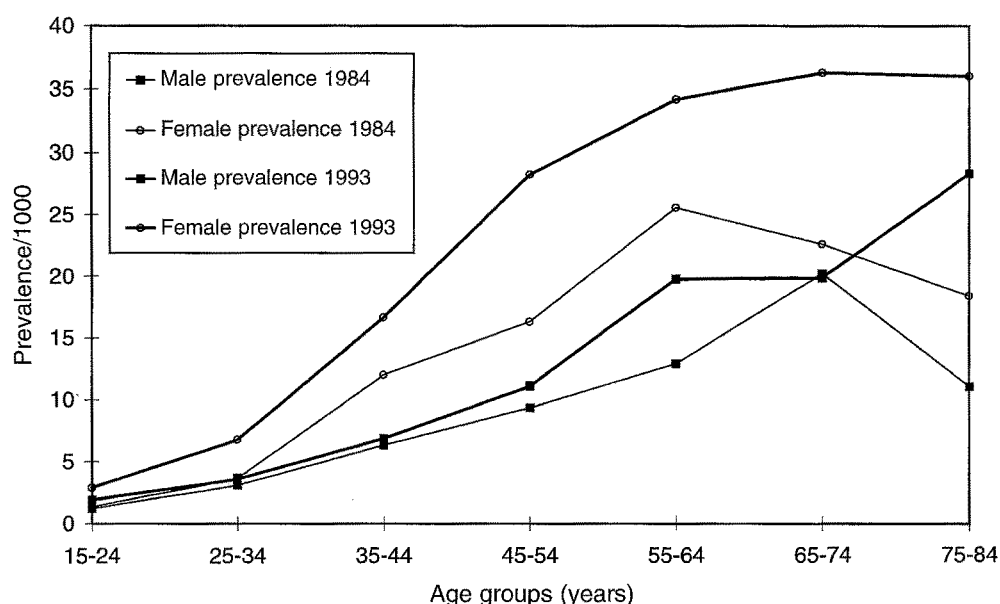
1984 and 1989. The increase was most marked among women as well as men over the age of 65 years (Fig. 2). In these age groups hypnotics were the only psychotropic medication prescribed to 40–50% of patients. Hypnotics are rarely prescribed to those under the age of 45 years, especially as the only psychotropic medication. However, there was a very marked decrease in the DDD/1000 per day of hypnotics from 1984 to 1989, particularly among women following new restrictions of prescribing hypnotics instituted in 1988.

The prevalence of antidepressant use has increased very markedly through both periods, especially among women. The quantity prescribed measured by DDD/1000 per day has increased by 75% among men and by over 100% among women. In 1989 13.7 DDD/1000 per day of tricyclics were prescribed and 1.1 DDD/1000 per day of

SSRI. In 1993 the quantities prescribed were 12.7 and 7.1 DDD/1000 per day, respectively. The increase in prevalence of treatment with antidepressants was most marked among women aged 65 years and more, reaching 3.6% in 1993, and among men 75 years or older (Fig. 3).

In order to evaluate further the effects of the administrative decisions regarding tranquilizers and hypnotics, and the introduction of the SSRI medications on the number of patients receiving prescriptions for psychotropic medications, the data was grouped according to the hierarchy described and shown in Table 3. The number and proportions of patients receiving neuroleptics or tranquilizers as the main medications decreased from 1984 to 1993, whereas those receiving antidepressants and hypnotics increased. As the gender and age distribution of patients obtaining the various drug groups changed between

**Fig. 3** One-month prevalence of patients obtaining antidepressants in Reykjavík in 1984 and 1993 by gender and age



**Table 3** Number of patients prescribed psychotropic medications. Hierarchical distribution by main type of medication and year

	1984 N (%)	1989 N (%)	1993 N (%)
Neuroleptics	467 (9.7)	411 (8.3)	419 (8.1)
Antidepressants	559 (11.6)	742 (14.9)	988 (19.1)
Tranquillizers	2443 (50.9)	2065 (41.6)	2027 (39.2)
Hypnotics	1333 (27.8)	1748 (35.2)	1731 (33.5)
Total <sup>a</sup>	4802 (100.0)	4966 (100.0)	5165 (99.9)

<sup>a</sup> Total figures are slightly lower than in the text as data are missing on some patients for the hierarchical ranking of the prescriptions

**Table 4** Prevalence odds ratios (95% confidence interval) of receiving psychotropic medications by main type of medication and year, adjusted by a log-linear model for gender, age, prescribing physician's speciality and two-way interactions

	1984	1989	95% CI	1993	95% CI
Neuroleptics	1	0.64	0.44–0.94	0.78	0.55–1.11
Antidepressants	1	0.96	0.77–1.20	1.51	1.07–2.14
Tranquillizers	1	0.66	0.45–0.95	0.74	0.52–1.04
Hypnotics	1	0.97	0.67–1.42	1.08	0.76–1.54

years, so did the distribution of prescriptions by speciality of the physicians. The data were fitted to a log-linear model in order to adjust for these changes. The prevalence odds ratio of patients aged 75 years or more for receiving psychotropic medications increased from 1984 to 1989 and 1993 (95% confidence limits in 1989 were 1.07–1.57 and in 1993 were 1.10–1.61). Table 4 shows the prevalence odds ratios of receiving each type of medication in the 3 years studied according to the model. The prevalence odds ratio of patients being prescribed neuroleptics and tranquillizers decreased in 1989, whereas the odds of patients obtaining antidepressants increased in 1993 and that of hypnotics alone remained unchanged.

## Discussion

Official sales figures of psychopharmacological drugs and prevalence estimates based on the number of patients filling their prescriptions overestimate the consumption due to non-compliance. However, neither should this nor other possible biases related to sampling affect the comparison of the results of the study, as the sampling procedure was identical in all 3 years.

Apart from clinical factors, such as symptoms and signs of psychiatric disorders, other elements strongly affecting the prescriptions of psychopharmacological drugs (Uhlenhuth et al. 1993; Kühlhorn and Leifman 1993; Joukamaa et al. 1995) are availability of effective medications, age, gender, attitudes of physicians and control measures.

The present study, like other studies (Isacson and Haglund 1988; Nolan and O'Malley 1988; Joukamaa et al. 1995), found the use of psychopharmacological drugs increasing with increasing age, especially of hypnotics and antidepressants, but to a lesser degree, of tranquillizers and neuroleptics. This is contrary to the results of epidemiological studies of mental disorders which for the most part do not support the notion of an increasing prevalence with age, except for cognitive impairment (Regier et al. 1988; Helgason 1991a) and complaints of insomnia (Kristbjarnarson et al. 1985; Mellinger et al. 1985). This indicates that the choice of treatment is dependent on the patient's age, or that younger people do not seek medical help for their mental disorders if they are not deemed severe enough to warrant seeing a psychiatrist. In this connection it should be recalled that the patients seen by psychiatrists are on average considerably younger than those seen by other physicians (Helgason 1992).

The gender differences in prevalence of psychopharmacological drug use and the total amount prescribed have remained fairly similar from 1984, except that the female: male ratio for antidepressants has increased, i.e. the prevalence for women was twice as high as that for

men in 1993. If substance abuse disorders are excluded, the gender differences in psychopharmacological drug use are found to be similar to those in epidemiological studies (Helgason 1991b), although they are somewhat more marked.

#### Effects of official restrictions

As can be seen from the results, the prevalence of psychopharmacological drug use is affected by control measures aimed at limiting the amount prescribed. Despite health authorities' attempts to contain the use of psychopharmacological drugs in particular that of tranquillizers and hypnotics, the total prevalence of psychopharmacological drug use has remained practically unchanged from 1984 to 1993, whereas the amount prescribed in DDD/1000 per day decreased by 8–9% from 1984 to 1989, but increased slightly again in 1993. However, the changes as regards hypnotics clearly follow public health authorities' attempts to curb their use. Following the restrictions imposed on prescriptions for hypnotics in 1988 (Heilbrigðis- og tryggingamálaráðuneytið 1988), the prevalence of persons obtaining hypnotics increased, especially in the older age groups, whereas the amount prescribed in DDD/1000 per day decreased. This could be taken to indicate that elderly people, who previously obtained prescriptions with supplies for 2 or 3 months' use, now have to see their general practitioners every month, as they can only obtain 30 DDD on each prescription. On the other hand, the log-linear model does not indicate any change in the prevalence odds ratio of people receiving prescriptions for hypnotics only (cf. Table 4). A dramatic reduction in the proportion of patients obtaining more than 30 DDD during 1 month could be seen in 1989, whereas there was some increase in the proportion of patients obtaining more than one prescription. There has been some decrease in the use of tranquillizers during the whole period, mainly between 1984 and 1989, reflected both by decreasing prevalence and decreasing DDD/1000 per day.

The policy of ending any reimbursement for tranquillizers and hypnotics in 1991 has neither affected the proportion of patients obtaining more than one prescription nor the number obtaining more than 30 DDD during the month nor the prevalence of patients obtaining these medications. The proportion of excessive users, defined as those obtaining more than 90 DDD of these drugs during 1 month, has decreased. The possible abuse of prescribed tranquillizers or hypnotics may be a public health problem, but is certainly much smaller than that resulting from the abuse of alcohol. The prevalence of excessive drug use as defined herein was 0.5% in 1993, whereas that of alcohol abuse was 4.6% in 1992 (Helgason et al. 1994).

#### Effects of the new antidepressants

The study shows an increase in the prevalence of treatment with antidepressants, more marked among women

than men, and an even greater increase in the quantity prescribed. The increase in prevalence is most marked among the elderly, probably indicating that doctors are more willing to prescribe the new antidepressants which have fewer side effects than the tricyclic antidepressants (American Psychiatric Association 1993). However, it is still debated whether compliance is better for the SSRI drugs (Hotopf et al. 1996).

The sale of antidepressants is considerably higher in Iceland than in the other Nordic countries (NOMESKO 1995), despite the prevalence of depressive disorders which are similar in these countries (Helgason 1990).

The increased antidepressant prescriptions in Reykjavík is not explained by an increase in prescriptions by any specific group of physicians as shown by the log-linear model which adjusts both for the number of prescriptions by different specialists and the varying age and gender distribution of their patients. The model shows an increase in the prevalence odds ratio of patients receiving antidepressants, but a non-significant decrease for receiving neuroleptics with or without antidepressants, and tranquillizers without antidepressants.

The increase in antidepressants has mainly been in the new SSRI and selective monoamine oxidase inhibitors (Heilbrigðis- og tryggingamálaráðuneytið 1993, 1996). These drugs have only to a limited extent substituted tricyclic antidepressants. However, it has to be considered that new indications for antidepressants have emerged, e.g. for the treatment of obsessive-compulsive disorders, chronic pain (Gilman et al. 1992; Eberhard et al. 1989) and chronic fatigue syndrome (Goodnick and Sandoval 1993). The increased prevalence of antidepressant prescriptions could also to some extent be related to the fact that reimbursement for tranquillizers and hypnotics is no longer available, leading some doctors to prescribe medications which are reimbursed, e.g. antidepressants, to relieve anxiety or insomnia.

#### Conclusion

It is quite obvious from the data presented that the restrictions on prescriptions for hypnotics have been effective in reducing the amount prescribed, but not the prevalence of those obtaining a prescription during 1 month. However, transferring the cost entirely to the patients has not been as effective and may have contributed to the increased use of antidepressants, which are partly paid for by the National Health Insurance. But this increase is mainly due to the introduction of new antidepressants.

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